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EVALUATION OF FSH, LH AND TESTOSTERONE LEVELS IN DIFFERENT SUBGROUPS OF INFERTILE MALES

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ABSTRACT

Gonadotropins (FSH, LH) and testosterone are the prime regulators of germ cell development. Abnormal spermatogenesis is often associated with altered serum gonadotropins and testosterone. FSH, LH and testosterone levels were estimated in 96 infertile men of whom 35 were azoospermic, 35 were oligozoospermic, 11 were with varicocele and 15 were with histopathological abnormalities like hypospermatogenesis, spermatid arrest and sertoli-cell only syndrome. Results showed statistically significant ($p< 0.05$) increase in the mean FSH and LH levels in all the infertile males studied when compared with the fertile controls (n=35). However, there is no significant difference in the mean levels of testosterone between the infertile and fertile men.

KEY WORDS

Male infertility, FSH, LH, Testosterone, Varicocele, Hypospermatogenesis, spermatid arrest, Sertoli – cell only syndrome

INTRODUCTION

The successful and complete male germ cell development is dependent on the balanced endocrine interplay of hypothalamus, pituitary and the testis. Gonadotropin releasing hormone (Gnrh) secreted by the hypothalamus elicits the release of gonadotrophins i.e follicle stimulating hormone(FSH) and lutenizing hormone(LH) from the pituitary gland (1). FSH binds with receptors in the sertoli cells and stimulates spermatogenesis. LH stimulates the production of testosterone in Leydig cells, which in turn may act on the Sertoli and peritubular cells of the seminiferous tubules and stimulates spermatogenesis (2).

The failure of pituitary to secret FSH and LH will result in disruption of testicular function leading to infertility. Testosterone, estradiol and inhibin control the secretion of gonadotropins (3). The increased FSH level in men with azoospermia or severe oligozoospermia (<5million sperm/ml) indicate damaged seminiferous tubule (4). Studies have shown that in infertile men with germinal epithelial injury, no stimulation of spermatogenesis occurs due to low or lack of production of androgen binding proteins. In addition the production of inhibin and testosterone, dihydrotestosterone and estradiol is affected causing disturbance in negative feed back mechanism resulting in elevated levels of FSH (5).

Although studies have been carried out on the role of FSH, LH and testosterone in infertile males, very few studies were carried out on hormonal levels in different subgroups of infertile males. Hence, an attempt has been made to estimate the gonadotropins (FSH, LH) and testosterone in infertile males with azoospermia, oligozoospermia, varicocele and infertile males with abnormal histopathological conditions like hypospermatogenesis, spermatid arrest and Sertoli – cell only syndrome.

MATERIALS AND METHODS

Ninety six infertile men (age group 31 – 35 years) with at least 3 years duration of infertility referred by various fertility centres and hospitals to the Institute of Genetics and Hospital for Genetic Diseases, Hyderabad were selected for the study. In all the cases, female partners were examined for their fertility using hormonal evaluation for ovarian function and laproscopy for the confirmation of tubal patency. Only those cases where the male partner whose female partner was found to be normal were selected for the study. Thirty five normal males (age group 31 – 35 years) belonging to the same socioeconomic status were selected as control group. The last pregnancy was observed 2-4 years back in the control group. The infertile and control subjects with STD's were excluded from the study.

Clinical examination of all the subjects was carried

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out and information on age, health problems, duration of marriage, history of infertility in the family, parity, etc was recorded. Semen was collected from the infertile subjects with three days of sexual abstinence. Estimation of sperm counting was done using the Meckler's chamber. Sperm analysis was carried out according to the World Health Organization (6) guidelines. Based on the sperm concentration the infertile subjects were classified as follows: Normozoospermia (> 20 million sperm /ml), Oligozoospermia (<20 million sperm/ml) and azoospermia (no spermatozoa). In proven fertile controls, the sperm count ranged from 20 –120 million sperm /ml. Doppler test was done and the grade of varicocele was recorded. Cytogenetic studies were carried out and only those cases with normal karyotype were included for the study. Testicular biopsy was carried out to understand the histopathological condition of the case.

FSH, LH and testosterone levels were evaluated in all the 96 infertile men and 35 age matched controls with proven fertility . For comparison, hormone levels were also evaluated in 5 controls (proven fertile men) with normal testicular histology. The hormonal assays were done by Radio Immuno assay (RIA) using the kits supplied by Diagnostic Products Corporation, USA. The results obtained were statistically analysed using students t-test and one way ANOVA.

RESULTS

The results on the types of subgroups and histopathological conditions and mean serum FSH, LH and testosterone levels in infertile and control (proven fertile men) groups are presented in tables 1 and 2. Out of 96 infertile men, 35 (36.4%) were azoospermic, 35 (36.4%) were oligozoospermic and 11 (11.4%) had varicocele of group I to III (Table 1). 15 out of 96 infertile males showed abnormal testicular histology. The cases include 5 subjects each of hypospermatogenesis, spermatid arrest and Sertoli – cell only syndrome (Table 2).

The mean serum FSH, LH and testosterone levels in the infertile and controls (proven fertile men) are presented in table-1. The mean FSH and LH levels (mIU/ml) in azoospermic infertile males were 12.60 ± 12.19 and 12.42 ± 9.86 respectively, whereas in oligozoospermic infertile males, the mean FSH and LH levels were 12.96 ± 9.36 and 15.05 ± 9.28 respectively as against 8.50 ±5.46 and 7.88 ±3.63 in controls respectively. FSH and LH levels showed significant increase ($p<0.05$) in both azoospermic and oligozoospermic infertile males. However, analysis of the data by one way ANOVA revealed no significant ($p > 0.05$) differences for FSH and LH levels in between different subgroups (azoo, oligo, and varicocele). The mean testosterone values in azoospermic and oligozoospermic group were 4.94 ± 0.98 ng/ml and 4.89 ± 0.95 ng/ml respectively while the testosterone level in the fertile control group was 5.01 ± 1.31 ng/ml. The differences for the mean testosterone levels between the proven fertile and infertile men with azoospermia and oligozoospermia were insignificant ($p>0.05$). While the mean FSH and LH levels were significantly increased ($p< 0.05$) in infertile males with varicocele when compared to the control values the mean testosterone level in infertile male with varicocele was comparable to the control value (Table 1).

Table 1: Serum FSH, LH and testosterone levels in different subgroups of infertile males

S.No.	Group	Number of Subjects	Hormone levels mean ± SD		
			FSH (miu/ml) (Range)	LH (miu/ml) (Range)	Testosterone (ng/ml) (Range)
1.	Fertile males (control)	35	8.50 ± 5.46 (3.21-22.28)	7.88 ± 3.63 (3.21-18.45)	5.01 ± 1.31 (3.18-8.27)
2.	Infertile males				
a.	Azoospermia	35	12.60 ± 12.19* (3.08-51.21)	12.42 ± 9.86* (2.09-46.75)	4.94 ± 0.98 (2.96-6.78)
b.	Oligozoospermia	35	12.96 ± 9.36* (3.94-42.64)	15.05 ± 9.28* (3.90-42.11)	4.89 ± 0.95 (2.91-7.25)
c.	Varicocele	11	20.29 ± 3.80* (4.29-21.59)	12.98 ± 7.36* (4.08-30.61)	5.07 ± 0.09 (3.88-6.82)

*$p<0.05$

Table 2: Serum FSH, LH and testosterone levels in fertile and infertile males with abnormal testicular histology

S.No.	Group	Number of Subjects	Hormone levels mean ± SD		
			FSH (miu/ml) (Range)	LH (miu/ml) (Range)	Testosterone (ng/ml) (Range)
1.	Fertile males with normal testicular histology (control group)	5	8.31 ± 0.60 (7.67-9.23)	8.45 ± 0.72 (7.52-9.25)	5.05 ± 0.40 (4.52-5.82)
2.	Infertile males with abnormal testicular histology				
a.	Hypospermatogenesis	5	13.35 ± 1.77* (11.02-15.62)	14.05 ± 0.61* (13.29-15.00)	4.90 ± 0.33 (4.35-5.23)
b.	Spermatid arrest	5	14.81 ± 1.80* (12.05-16.98)	14.91 ± 1.34* (13.29-15.00)	5.05 ± 0.12 (4.89-5.23)
c.	Sertoli - cell only syndrome	5	20.29 ± 3.80* (15.72-24.33)	19.98 ± 1.48* (17.75-21.92)	5.30 ± 0.56 (4.82-6.23)
	Total (a+b+c)	15	16.15 ± 3.94*	16.03 ± 3.03*	5.08 ± 0.39

*$p<0.05$

The mean serum FSH, LH and testosterone levels in infertile males with abnormal testicular histology are presented in table-2. In infertile men with abnormal testicular histology the mean FSH value was 16.15 ± 3.94 mIU/ml as against 8.31 ± 0.60 mIU/ml in proven fertile controls. The mean values of FSH were 13.35 ± 1.77, 14.81 ± 1.80 and 20.29 ± 3.80 mIU/ml in hypospermatogenesis, spermatid arrest and Sertoli-cell only syndrome respectively. The FSH levels in all the subgroups of infertile males with abnormal testicular histology were significantly increased ($p<0.05$) when compared with the controls. The mean LH value (mIU/ml) in control group was 8.45 ± 0.72 and it has increased to 16.03± 3.03 infertile males with abnormal testicular histology. In hypospermatogenesis, spermatid arrest and Sertoli-cell only syndrome condition the LH values (14.05 ± 0.61, 14.91 ± 1.34 and 19.98 ± 1.48 mIU/ml) were higher when compared with the control values ($p<0.05$).

The mean testosterone level in the infertile males with abnormal testicular histology (5.08 ± 0.39 ng/ml) was comparable with the control value (5.05 + 0.39ng/ml. P> 0.05) (Table-2).

DISCUSSION

FSH, LH and testosterone evaluation is useful in the management of male infertility (7). For initiation of spermatogenesis and maturation of spermatozoa, FSH is necessary. In the infertile men, higher concentration of FSH is considered to be a reliable indicator of germinal epithelial damage, and was shown to be associated with azoospermia and severe oligozoospermia (4). de Kretser *et al.* (8) reported elevated levels of serum FSH with increasing severity of seminiferous epithelial destruction.

In the present study, gonadotropin (FSH and LH) levels were significantly elevated in infertile males when compared with the levels in proven fertile controls. These results are in accordance with the studies of Sulthan *et al.* (9). Zabul *et al.* (7), Weinbaurer and Nieschlag (10), and Subhan et *al.* (11) who showed elevated levels of both follicle stimulating hormone and luteinizing hormones in infertile males. Elevated levels of LH in oligozoospermic and azoospermic males when compared to normal fertile men were also reported (12-13). In the present study the difference in the mean serum testosterone levels between fertile and infertile men were insignificant. Similar observations were made by Smith *et al.* (14) and Subhan *et al.* (11).

In the present study, the mean serum FSH and LH levels were significantly elevated in infertile men with varicocele when compared with the controls. Rege *et al.* (15) and Gorelic and Goldstein (16) showed elevated serum FSH levels and Nagao *et al.* (17) showed elevated levels of LH in infertile men with varicocele.

In infertile males with abnormal histopathology (Sertoli-cell only syndrome, hypo spermatogenesis, and spermatid arrest), the mean FSH levels were significantly elevated compared to the control group. Yanam *et al.*, (18) also showed a significant increase

in the mean FSH levels in infertile males with Sertoli-cell only syndrome, hypo spermatogenesis and maturation arrest. Micic (19), Nistal *et al.* (20) and Turek *et al.* (21) also showed significantly elevated mean FSH levels in infertile males with Sertoli-cell only syndrome. However, Weiss *et al.* (22) reported insignificant increase in the mean FSH levels in infertile men with Sertoli-cell only syndrome.

In the present study, LH levels were higher in infertile males with Sertoli-cell only syndrome. These results are in agreement with Micic (19) who also showed elevated levels of LH in infertile males with Sertoli-cell only syndrome. However, some studies (20,21,23) showed normal levels of LH in infertile males with Sertoli-cell only syndrome.

The testosterone levels in the infertile men with Sertoli-cell only syndrome were found to be normal (Table-2). The studies of Micic (19) Nistal *et al.*, (20) and Turek *et al.*, (21) also reported normal testosterone levels in infertile men with Sertoli-cell only syndrome.

FSH, LH and testosterone are prime regulators of germ cell development. The quantitative production of spermatozoa generally requires the presence of FSH, LH and testosterone. FSH acts directly on the seminiferous tubules whereas luteinizing hormone stimulates spermatogenesis indirectly via testosterone. FSH plays a key role in stimulating mitotic and meiotic DNA synthesis in spermatogonia (24).

The colour doppler study ruled out ductal obstruction. All the subjects were normal individuals and their chromosome analysis did not present any evidence for abnormal karyotypes. In addition, there is no family history of infertility in the cases studied and hence the infertility in these cases might be attributed to hormonal causes. The overall results clearly indicate significant increase in gonadotropins (FSH and LH) in all the subgroups (azoospermia, oligozoospermia, varicocele) and also in infertile males with abnormal testicular histology. Although there was no significant decrease in the testosterone levels in infertile males when compared with the fertile controls, the increase in the levels of gonadotropins might have disrupted the spermatogenic process leading to the decline in the sperm count and infertility.

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